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Developmental Basis of Behavior

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MOST GENETIC mutations that effect an evolutionary change in adult characters, behavioral or morphologic, do so indirectly by affecting the process of development. Evolutionary change must in a sense be funneled through the developmental mechanisms. In many cases it may be these latter, rather than chromosomal plasticity or selection pressures on the adult character, that constitute the limiting conditions in evolution and determine the direction in which it moves. Given two possible character changes of equal functional survival value, one achieved easily in terms of developmental adjustments, the other involving radical revisions of the growth pattern, it is the former that will be favored. Many evolutionary possibilities that would be entirely feasible so far as survival value and genetic mutability are concerned can never be realized because they could not be achieved within the established framework of embryonic development. Many aspects of evolution are better understood with some consideration for the developmental processes through which, and in terms of which, the genetic mutations must operate.

From the developmental standpoint it is helpful to think of the evolution of behavior in terms of the evolution of the morphological structures that mediate the behavior. The term "structure" may be used here in its broadest sense to include all stable organization patterns of organs and tissues, even at submicroscopic and molecular levels. The inheritance of a behavior pattern then implies the inheritance of certain modifications of the behavioral apparatus responsible for the behavior. The distinction between behavioral and morphological in inherited characters is hardly a basic one from the viewpoint of development. Accordingly, the present discussion will be concerned largely with development of the inherited morphological substrate of behavior, primarily that of the sensorineuromotor apparatus, with special emphasis on the patterning of interneuronal connections in the central nervous system. The subject will be treated not entirely from the perspectives of embryology, but with reference more to the problem of effecting evolutionary change in developmental mechanics.

Generally speaking, gene action during development may and most commonly does occur at many removes from the observed character effect. According to one current theory, gene changes within the nucleus lead to changes in cytoplasmic RNA (ribonucleic acid), which in turn modify protein synthesis, thereby producing alterations in enzyme activity, with consequent effects on cell metabolism and cell differentiation (Horowitz and Fling, 1956). These, in turn, modify organ and tissue development to determine ultimately the observed character change. In view of the numerous levels of organization involved in this chain of events, ranging from that of the gene unit up to the level of the adult nervous, circulatory, and hormonal systems; and in view of the numerous types of potential interaction within and among all these various levels of organization, the possible patterns of causal sequence by which a gene mutation may affect a change in behavior are, for practical purposes, almost infinitely varied. Some inherited characters like pigmentation, enzymatic properties, and inherent immunologic specificity may reflect the genetic mutation rather directly. Behavioral traits on the other hand appear to be at the other extreme where the sequence of developmental events between gene change and behavioral change is a long and devious one and one that, at the present state of our knowledge, can be discussed for the most part only in broad generalities.

It should be recognized at the outset that much remains to be learned with respect to the old problem of the extent to which behavior mechanisms are a product of inheritance on the one hand and of learning and experience on the other. Since the learned and the inherited elements in behavior are frequently present together as inseparable cofunctions, it is difficult or impossible in many cases to evaluate the relative extent and significance of the separate factors. This is particularly true when there is a long period of neural growth and maturation during which learning is also taking place, as in man. However, if we consider the problem with refer-

ence strictly to the anatomy, physiology, and growth of the apparatus of behavior, there are some inferences that may be drawn with respect to the vertebrate nervous system in general.

The entire nervous structure, including all the fiber circuit organization demonstrable by the methods of neuroanatomy, is, by and large, a product of growth and inheritance, not of learning. To this anatomically demonstrable structure we must add the mechanisms underlying much organization that is demonstrable only by physiological and behavioral methods. Included here would be all or nearly all the functional organization of the brain stem and spinal cord. Much of the functional organization of the cerebral hemispheres must also be included even in man. For example, all the effects produced by stimulation of the primary sensory and motor areas of the cortex along with other similar effects that are species-constant must be included with the inherited bases of behavior.

Approaching the question from the other direction, one may say that the entire neural apparatus is organized through the forces of growth and inheritance except for the as-yet-undemonstrated memory traces or engrams. Whatever the neural changes of learning and memory may be, they are extremely elusive and inconspicuous and have yet to be demonstrated in any direct manner. Presumably they are infused into or are superimposed upon the more out-of-the-way neural circuits, particularly in the mammalian cerebral cortex. Although the experientially produced mutations in the neural apparatus may make a large and important difference at the behavioral level, they appear to be only a minute fraction of the total neural organization from the anatomical and developmental standpoint. It seems probable that the underlying inherited portion of the neural mechanism involved even in so-called "learned" behavior may be not only more conspicuous but also much more complex in its organization, anatomically and physiologically speaking, than is the superimposed experiential portion of the structure.

The foregoing represents a radical change from earlier views which had pictured the functional patterning of neural circuits as being achieved almost entirely through training and experience (Holt, 1931). Prior to the late 'thirties it was supposed that the outgrowing nerve fibers established their connections in a haphazard, diffuse, and excessive fashion in development tending to form initially an equipotential homogeneous network out of which adaptive pathways were subsequently channeled by means of function. A related view pictured the initial tendency to form excessive central connections as being functionally controlled, the fiber connections that happened to prove adaptive being reinforced and maintained, the nonadaptive ones being eliminated through disuse atrophy, and degeneration. This functional molding of the neural circuits was presumed to begin at the first evidence of neuromotor activity and to continue in the mammal through fetal life into postnatal learning. Common reference was made to the training of the sensory surfaces such as the cutaneous and retinal fields, the macula of the utriculus, the proprioceptors of posture and movement and the like.

Today we think the developing nerve fibers establish their synaptic associations in a highly specific manner from the very beginning. The outgrowing fibers of the developing neuroblasts are believed to form well-organized reflex and integrative patterns that are functionally adaptive from the start but which nevertheless are patterned directly in the growth process. This change in the picture of nervous development is supported by an extended series of observations in which surgical disarrangement of the adult and developing nervous system in many different vertebrates has been found to produce corresponding dysfunctions that persist in machine-like fashion uncorrected by experience (Sperry, 1945; Weiss, 1941). The more recent findings along this line have contradicted earlier reports which had indicated that the vertebrate nervous system was highly plastic in this respect. More direct support for the current concepts derives from investigations dealing with the formation of synaptic connections during nerve regeneration and development. These latter show the normal patterning of synaptic relations to be predetermined in the growth process irrespective of the functional effects for the individual.

The patterning of refined and precisely adapted behavioral patterns has been shown in these studies to be developmentally controlled, and in some cases the experiments yield information about the nature of the growth forces involved. These will be considered later. In general the developmental mechanisms, as we now picture them, appear to be of sufficient specificity and elaboration that one need not hesitate, on the basis of complexity alone, to ascribe to inheritance any behavior pattern found among subhuman verte-

brates. One gets the impression that no vertebrate behavior pattern, excepting perhaps language and certain other of the more complicated human activities, is too complex to be built into the nervous system so far as the proficiency of the developmental and genetic mechanisms is concerned. Where the behavior pattern is acquired by learning instead of being handled through inheritance, one may assume this to be a result of other factors rather than a limitation in developmental capacity. These changes in neuroembryological theory have profound implications for the evolution of behavior and for all concepts relating to the role of inheritance in behavior.

Inherited behavioral changes in the nervous system are presumably traceable to changes in the size, number, connectivity, and excitatory properties of the nerve cells. Actually changes in neuron size and number gain their functional effects mostly through secondary influences upon connectivity and excitatory threshold. Our problem centers therefore around the developmental mechanisms responsible for the establishment of excitatory thresholds in nerve cells and for the patterning of their fiber connections. To review here all the known information relating to these matters would be impossible. Extensive descriptions of the gross and microscopic morphogenesis of the nervous system may be found in the textbooks of neurology and embryology. In particular, reference should be made to the expanding literature on experimental analysis of the underlying developmental forces in ontogeny (Willier, Weiss, and Hamburger, 1955).

The resting excitatory threshold and also the interconnections of neurons appear both to depend largely upon specific cell properties attained through gradual differentiation of the nerve cells in development. The process of embryonic cell differentiation, after it has succeeded in setting off future nerve cells from those of muscle, bone, and other tissues, continues to effect differentiation within the nerve cell population itself. As a result the different classes and types of neurons become intrinsically different from one another in constitution. In some parts of the nervous system the process of differentiation continues almost to the point where the individual neurons differ from one another in quality. The resting excitatory threshold characteristic of the different neuron types would seem to be an important factor in neural integration. That it is determined through the differentiation process would

seem a safe assumption. However, for lack of evidence there is little more that one can say about the threshold factor at present.

Much more information is available with respect to the role of connectivity in neural function and the developmental forces responsible for the patterning of neuronal interconnection. According to classical neurophysiology the differential fiber connections among nerve cells are of paramount importance and the basis of functional organization. Various other concepts of central nervous integration have been proposed, such as those based on mass electric fields, specific nerve energies, frequency effects, and resonance phenomena. None of these has received sufficient support to warrant its replacing the conventional connectivity doctrine as a basis for our present discussion. Furthermore numerous illustrations of the dysfunction produced by surgical disarrangement of the normal nerve connections have given convincing demonstration of the direct dependence of neural integration upon selective specificity in neuronal connections.

The establishment in development of the proper synaptic connections for any given nerve cell must typically depend upon a host of factors, direct and indirect, including proper timing of the developmental sequence. It would be impossible to consider the whole picture here, and the reader is referred again to the textbooks on descriptive and experimental embryology. The present discussion is limited to brief mention of some of the factors that appear to be most directly responsible for regulating the formation of proper synaptic relations.

These are best illustrated by reference to a concrete example such as the genesis of cutaneous local sign. For the accurate localization of points on the body surface it is necessary that the central reflex relations of the cutaneous fibers match accurately their peripheral connections. When this is not the case, as after the misdirection of regenerating cutaneous fibers into foreign skin, the result is a corresponding false reference of sensation. In a sense, accurate localization requires that the central connections of the cutaneous fibers reflect in an orderly way the entire map of the body surface. Anatomically it is well established that the topography of the body surface is mapped on the various sensory relay stations of the CNS, i.e. the gracilis and cuneate nuclei, the ventral nucleus of the thalamus, the postcentral gyrus of the cerebral cortex, and also on the cerebellar cortex.

The way in which the orderly anatomical arrangement of this cutaneous system is achieved in development has been investigated to a small extent (Miner, 1951; Sperry, 1954) and would seem to be something as follows: An initial outgrowth of cutaneous fibers into the skin leads to terminal connections that are largely random within each dermatome. The integument meantime undergoes an early field-type differentiation that sets off dorsal from ventral skin and head from tail skin. This is believed to be achieved through the establishment of two embryonic gradients of differentiation, an anteroposterior and a dorsoventral gradient, laid down at right angles to each other. As a result of these two axes of differentiation, each cutaneous spot on the body surface becomes marked by a combination of two gradients giving it a latitude and longitude, so to speak, that is unique for each individual spot on each side of the body.

Experiments have shown that the local topographic specificity of the integument becomes impressed in some form upon the cutaneous fibers through their terminal contacts. The specificity stamped on the terminals of the cutaneous fibers then spreads throughout the extent of the nerve cell. In the case of the sensory neurons of the hind limb, for example, this means a spread centrally into the lumbar dorsal root ganglia and along the dorsal roots into the cord. Within the cord the qualitative specificity spreads along the posterior columns for long distances, particularly rostrally where many fibers extend all the way to the nucleus glacilis at the base of the medulla. Within the latter nucleus and at all segmental levels along the cord, the specificity factor must spread also into the fine collateral fibers that arborize within the gray matter to form synaptic connections with the second order sensory neurons.

The local sign specificity that is stamped upon the cutaneous fibers at the periphery and is spread thus centrally into all the growing tips of the finest central collaterals is presumed to determine the type of second order neurons which the growing tips will find acceptable for synapsis. This inference implies the existence of a similarly refined qualitative specificity among the central neurons. Presumably the cutaneous centers of the medulla, thalamus, and cortex undergo self-differentiation, in such a way that the qualitative properties of the neurons become distributed in an orderly pattern with reference to the dermatomes of the body.

Fibers from one nucleus growing into the next higher center presumably have selective tendencies to establish synaptic linkages in the proper part of the nucleus or cortical area into which they grow. Mechanical and other developmental forces are also involved all along the way, particularly in guiding the fibers from one central station to the next.

The foregoing example includes several principles that appear to have rather general applicability, namely: the initial self-differentiation of the end organ, the induction of local specificity in the peripheral nerves through terminal contact with the end organ, the self-differentiation of central neurons, and the regulation of synaptic formation on the basis of specific chemical affinities between the various types of differentiated neurons. Perhaps the central concept here from the standpoint of evolution is that the inherent neuronal connectivity is determined through specific chemical affinities between the different classes of neurons and that these affinities arise out of processes of cell differentiation which are controlled ultimately through gene action. The fact that the particular patterns of chemical affinity that happen to arise in development are just the ones needed to produce circuit connections that are functionally adaptive is attributable to evolutionary selection and related factors in the same manner as is the adaptability of all developmental processes.

The interneuronal affinities are not simple one-to-one relations. Muscle proprioceptive fibers, for example, establish excitatory synaptic relations with the motorneurons of their own muscles and with a variety of internuncials leading to synergic muscles and apparently also inhibitory synapses leading to antagonistic muscles (Lloyd, 1955). In addition the proprioceptors establish connections leading into the ascending cerebellar tracts and into the dorsal columns. It would seem to be the rule rather than the exception that neurons have affinities for a variety of other neuron types. It is not inconceivable that the synaptic predispositions shown by a given fiber may be conditioned by its surroundings and may thus differ as the elongating fiber enters different regions of the central nervous system. These predispositions might differ also with time as the neuron goes through successive phases of maturation. In any case there would appear to be little or no limit to the complexity of neuronal interconnections possible in principle with this kind of scheme.

Many, but not all, behavioral changes in evolution are accompanied by correlated changes in the nonneural sensory and motor apparatus. Often the modifications in the peripheral apparatus are just as critical or more so than those in the central nervous system. Actually one could take almost any phase of development and show it to be important for behavior. The embryonic determination of such things as length of limb bones, size and strength of flight muscles, size and efficiency of endocrine glands, curvature of cornea and lens, even oxygen capacity of hemoglobin, and so on, can all be shown to have more or less direct influence on behavior and its survival value.

In regard to the question of which evolves first, the central nervous behavior pattern or the peripheral apparatus with which to carry it out, it must be a hen-egg type of relationship for the most part with concomitant development of both being necessary. However, from the standpoint of development, the central nervous patterns would seem to be the more difficult to evolve and therefore to constitute more of a limiting factor in evolutionary change. This is not necessarily true of the simpler neural changes that involve only the primary sensory and motor pathways or isolated central nuclei and affect merely numbers of neurons and/or their thresholds. It applies mainly to higher level integrative mechanisms involving complex and widespread interneuronal connections.

The course of cell differentiation in ontogeny may be visualized in a dendritic pattern like the evolution of species in phylogeny. It is then apparent that a developmental change that affects only one or a few closely related terminal twigs in the ontogenetic tree should be easier to initiate and to establish than one which requires coordinated changes in many widely separated branches. Apparently "simple" morphologic changes frequently depend upon numerous integrated alterations of the development process. In the case of a complex pattern of central nervous integration the complications are multiplied manyfold. The evolution of a complex instinctive behavior pattern such as that of nest building, for example, must involve a scattered array of adjustments in many areas of the brain. These could not all spring full blown from a single gene mutation. Changes in one nucleus must be made with reference to those in other nuclei. The whole central nervous pattern must therefore be put together step by step in the course of

evolution, each genetic change being made in terms of and with reference to all the others.

With regard to the interrelation of genetic mutations in effecting a coordinated pattern of morphologic change, it should be remembered that genes tend to control development through processes that already are intrinsically adaptive by nature. For example, the fact that eye size is right for orbit size in any species is not achieved by separate genetic control of the absolute size of each. It can be shown that the orbit will adjust itself through a considerable range to fit the sizes of eyes transplanted from other species (Twitty, 1932). This kind of thing occurs all through development. An enlargement of the eye and optic nerve will tend to produce a corresponding enlargement of the optic lobe in the midbrain through the stimulating effect of optic fiber ingrowth upon optic lobe development (Kollros, 1953). The sensory and motor nuclei in general tend to adjust in size to changes in the size of the peripheral load they come to innervate.

Many new developmental problems are associated with the evolution of learning capacity. Since the neural basis of learning is still unknown, there is little that can be said about the developmental processes by which it is installed in the brain. Perhaps it is a matter of increasing the number of association neurons; perhaps of increasing the number of fiber connections per neuron; or perhaps primarily of increasing some type of cytoplasmic plasticity in the nerve cells—or perhaps it is none of these, or that a combination of several such factors with others is required.

Where a given behavior pattern could be organized in development either by learning or by inheritance, one would expect, other things equal, that learning would be favored because it is more plastic and adaptable and therefore should have greater survival value. This would not apply to that background of neural organization that exists as a common denominator invariant in the behavior of all members of a species. The centering reactions of the optic system and the oculogyric reflexes might be examples. There would be no survival value in relegating the development of such to the sphere of learning since there normally is no call for adaptive alterations in these circuits. On the other hand, it is conceivable that, once the learning capacity of a species were sufficiently evolved, it might be easier and more economical from the stand-

point of developmental mechanics to drop the genetic support in time and gradually turn the organization task over to learning.

One might infer further that with a sufficiently increased learning capacity all inherent organization could be dropped and all behavioral organization be assigned to the learning process. If it is true, and it seems highly probable, that a rather elaborate and precisely designed neural mechanism is a prerequisite for learning, then the foregoing would be logically impossible. An organized background of neural organization has to be installed in advance by genetically controlled forces before new adaptive behavior patterns can be selected and nonadaptive ones eliminated by process of learning.

Generally speaking, however, it is to be expected that, once the learning capacity has evolved to a certain degree as in the higher primates, further evolution will tend to take the form of increased development of learning capacity rather than of further elaboration of instinctive behavior patterns. This would hold until learning and its effects became so powerful (as in human society) that physiological survival value no longer figures as an important limiting factor. At this point entirely new man-made principles of evolution appear and anything can happen.

For something like imprinting to occur, an elaborate preparation must be made through purely innate developmental mechanisms. Some brains are inherently so organized in growth that imprinting can occur; others are not. The capacity for imprinting must evolve through developmental mechanics just as do fully structured instincts.

The developmental basis of behavior becomes particularly complicated where the normal development or maturation process overlaps early learning. Under these conditions the effects of learning and maturation may be combined in many forms. Furthermore function may also be important as a general nonspecific factor that prevents atrophy from lack of use.

In the evolution of social behavior additional orders of complexity enter the picture in that the evolution of behavior patterns in each sex, caste, or other subgroup have to wait on the concurrently evolving behavior of other members of the group. Although this may not add new problems from a strictly developmental viewpoint, it does multiply those mentioned.

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(Star indicates general background reference.)

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